

4. (Amended) A process for fragmenting and labeling a synthetic or natural DNA or RNA nucleic acid, comprising the steps of:

chemically fragmenting said nucleic acid in the presence of at least one multivalent metal cation in an aqueous solution, to produce a plurality of DNA or RNA fragments having freed terminal phosphates for further reaction;

attaching a labeling agent on a plurality of said fragments at freed terminal phosphates located at the 3' end and/or 5' end of said fragments; and

treating said aqueous solution to decrease or eliminate unattached labeling agent.

15. (Amended) The process according to claim 7, wherein the treating step precipitates the labeled nucleic acid fragment at ambient temperature from a solution that contains betaine, dodecyl trimethylammonium bromide (DTAB) and unlabeled nucleic acid.

25. (Amended) The process according to claim 23, wherein the chemical catalyst is selected from the group consisting of N-methylimidazole, 3-(N-morpholino) propane sulfonic acid (MOPS), N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES), piperazine-N,N'-bis (2-ethane sulfonic acid) (PIPES), and bioorganic polyamines.

26. (Amended) A process for fragmenting and labeling a synthetic or natural DNA or RNA nucleic acid, comprising the steps of:

chemically fragmenting said nucleic acid in the presence of at least one multivalent metal cation selected from the group consisting of  $\text{Ba}^{2+}$ ,  $\text{Be}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Ce}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Eu}^{3+}$ ,  $\text{Fe}^{2+}$ ,  $\text{In}^{3+}$ ,  $\text{Lu}^{3+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Ru}^{3+}$ ,  $\text{Sr}^{2+}$ ,  $\text{Tb}^{3+}$ ,  $\text{Tm}^{3+}$  and  $\text{Yb}^{3+}$  in an aqueous solution to produce a plurality of DNA or RNA fragments having freed terminal phosphates for further reaction; and

attaching a labeling agent on a plurality of said fragments at freed terminal phosphates located at the 3' end and/or 5' end of said fragments.

Please add new claims 38 and 39 as follows:

--38. (New) The process according to claim 1, wherein the synthetic or natural member is DNA polymer.--

--39. (New) The process according to claim 26, wherein the synthetic or natural nucleic acid is DNA.--

REMARKS

Claims 1-39 are pending herein. By the Office Action, claims 1, 19, 22-37 are rejected under the judicially created doctrine of obviousness-type double patenting; claims 1-37 are rejected under 35 U.S.C. §112, second paragraph; claims 1, 2, 4-8, 10-15 and 19-37 are rejected under 35 U.S.C. §103(a). By this Amendment, claims 1, 3, 4, 15, 25 and 26 are amended, and dependent claims 38 and 39 are added. No new matter is added.

The attached Appendix includes marked-up copies of each rewritten claim (37 C.F.R. §1.121(c)(1)(ii)).

**I. Rejection for Obviousness-Type Double Patenting**

Claims 1, 19 and 22-37 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-2, 5, 7, 16-19, 22, 24 and 26-35 of U.S. Patent No. 6,376,179. Applicants respectfully traverse the rejection.

**A. Claims 1, 19, 22-25 and 33-37**

Independent claim 1 is drawn to a process for fragmenting and labeling DNA and chimeric DNA-RNA polymers that includes chemically fragmenting the polymer to produce a plurality of fragments and attaching a labeling agent on the fragments. The cited claims of the '179 patent do not teach or suggest such a process.

The cited '179 claims limit the claimed subject matter to RNA only. In particular, independent claims 1, 22, 26, and 30 all recite in part: "[A] process for labeling a synthetic or